

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF MAILING

I hereby certify that this REQUEST and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date indicated below with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450; Alexandria, VA 22313-1450.

Ariel Fletcher

Ariel Fletcher

12/29/2003
Date of Deposit

Applicant: Brooks, et al.

Serial No.: 09/081,522

Filed: May 19, 1998

Title: INHIBITION OF ANGIOGENESIS
IN DISEASE STATES WITH AN
ANTI- $\alpha\text{v}\beta 3$ MONOCLONAL
ANTIBODY (AS AMENDED)



Group Art Unit: 1644

Examiner: P. Gambel

Confirmation No. 1607

Our Ref.: TSRI 419.0 Con 1

FOURTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. §1.56 and §1.97

In accordance with the continuing duty of disclosure imposed by 37 C.F.R. § 1.56 and § 1.97 to inform the Patent Office of all references coming to the attention of each individual associated with the filing or prosecution of the subject application, which are or may be material to the patentability of any claim of the application, Applicants hereby direct the Examiner's attention to the references listed on the attached revised form PTO-1449 entitled "List of References Cited by Applicant." A legible copy of the fifteen attached references are being submitted herewith.

Identification of the listed references is not to be construed an admission of Applicants or Attorneys for Applicants that such references are available as "prior art" against the subject application.

Applicants respectfully request that the Examiner review the foregoing references and that the references be made of record in the file history of the application.

Since this Supplemental Information Disclosure Statement is being filed before the mailing date of the first Office Action after the filing of a Request for Continued

Examination under §1.114, the fee required to be filed with the accompanying Supplemental Information Disclosure Statement has been estimated to be \$0.00. However, should the Patent Office determine otherwise, please charge the required fee to Deposit Account No. 19-0962. A copy of this sheet is enclosed for accounting purposes.

December 29, 2003

Date

THE SCRIPPS RESEARCH INSTITUTE
Office of Patent Counsel
10550 North Torrey Pines Road
Mail Drop TPC-8
La Jolla, California 92037
(858) 784-2937

Respectfully submitted,



Thomas Fitting, Reg. No. 34,163

LIST OF REFERENCES CITED BY APPLICANT

(Use several sheets if necessary)

ATTY DOCKET NO.

TSRI 419.0 C1

APPLICATION NO

09/081,522

APPLICANT

Brooks et al.

FILING DATE

05/19/98

GROUP

1644

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A01	5,578,704	11/26/96	Kim			
	A02	5,652,109	7/29/97	Kim			
	A03	5,652,110	7/29/97	Kim			
	A04	5,677,181	10/14/97	Parish			
	A05	5,874,081	02/23/99	Parish			

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
	B01	WO 94/10331	5/11/94			YES NO

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

C01	Adams et al., "Increased Affinity Leads to Improved Selective Tumor Delivery of Single-Chain Fv Antibodies," <u>Cancer Research</u> 58: 485-490 (1998).
C02	Carmeliet, "Integrin indecision," <u>Nature Medicine</u> 8: 14-16 (2002).
C03	Cheresh, "Human endothelial cells synthesize and express an Arg-Gly-Asp-directed adhesion receptor involved in attachment to fibrinogen and von Willebrand factor," <u>Proc. Natl. Acad. Sci. USA</u> 84: 6471-6475 (1987).
C04	Cheresh et al., "Integrin-mediated death: An explanation of the integrin-knockout phenotype?" <u>Nature Medicine</u> 8:193-194 (2002).
C05	Posey et al., "Pilot Trial of Vitaxin, A Humanized Anti-Vitronectin Receptor (anti $\alpha_v\beta_3$) Antibody in Patients with Metastatic Cancer," <u>Cancer Biotherapy & Radiopharmaceuticals</u> 16: 125-132 (2001).
C06	Rader et al., "Phage display approach for rapid antibody humanization: Designed combinatorial V gene libraries," <u>Proc. Natl. Acad. Sci. USA</u> 95: 8910-8915 (1998).
C07	Reynolds et al., "Enhanced pathological angiogenesis in mice lacking β_3 integrin or β_3 and β_5 integrins," <u>Nature Medicine</u> 8: 27-34 (2002).
C08	Schier et al., "Isolation of High-affinity Monomeric Human Anti-c-erbB-2 Single chain Fv Using affinity-driven Selection," <u>J. Mol. Biol.</u> 255: 28-43 (1996).
C09	Schier et al., "Isolation of Picomolar Affinity Anti-c-erbB-2 Single-chain Fv by Molecular Evolution of the Complementarity Determining Regions in the Center of the Antibody Binding Site," <u>J. Mol. Biol.</u> 263: 551-567 (1996).

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.